

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 09 May 2001 (09.05.01)	
International application No. PCT/US00/17813	Applicant's or agent's file reference 1328 WO
International filing date (day/month/year) 28 June 2000 (28.06.00)	Priority date (day/month/year) 29 June 1999 (29.06.99)
Applicant DYSZLEWSKI, Mary, M. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

26 January 2001 (26.01.01)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Catherine Massetti Telephone No.: (41-22) 338.83.38
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PCT JUN 20 2002

REC'D 16 APR 2002

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

10/030741

Applicant's or agent's file reference 1328 WO		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/17813	International filing date (day/month/year) 28 June 2000 (28.06.2000)	Priority date (day/month/year) 29 June 1999 (29.06.1999)	
International Patent Classification (IPC) or national classification and IPC IPC(7): CO7F 13/00 and US Cl.: 534/14			
Applicant MALLINCKRODT INC.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 26 January 2001 (26.01.2001)		Date of completion of this report 22 March 2002 (22.03.2002)	
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer D. L. Jones Telephone No. (703) 308-1235	

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-22 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 23-25, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the drawings:
pages 1-5, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/17813**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>8, 12-16, 27, and 28</u>	YES
	Claims <u>1-7, 9-11, and 17-26</u>	NO
Industrial Applicability (IA)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-28 meet the criteria set out in PCT Article 33(4) because all the claims have industrial applicability.

Claims 1, 6, and 7 lack an inventive step under PCT Article 33(3) as being obvious over Alberto et al (J. Am. Chem. Soc., 1998, Vol. 120, pages 7987-7988) because Alberto et al disclose an organometallic complex of technetium useful for labeling biomolecules. The complex $[^{99m}\text{Tc}(\text{OH}_2)_3(\text{CO})_3]^+$ is generated in the presence of NaBH_4 . In addition, Alberto et al disclose complexes having the formula, $[\text{ReX}(\text{L})(\text{CO})_3]$ wherein L is a DNA intercalating ligand (see entire document, especially, page 7987). Hence, both Applicant and Alberto et al disclose a method of preparing a compound encompassed by formula I as set forth in Applicant's independent claim 1.

Claims 1-3 lack an inventive step under PCT Article 33(3) as being obvious over Alberto et al (Journal of Organometallic Chemistry, 1995, Vol. 493, pages 119-127) because Alberto et al disclose organometallic complexes of technetium and rhenium having the formula $[\text{NEt}_4]_2[\text{MCl}_3(\text{CO})_3]$ generated in the presence of BH_3 -tetrahydrofuran (see entire document, especially, abstract). Hence, both Applicant and Alberto et al disclose a method of preparing a compound encompassed by formula I as set forth in Applicant's independent claim 1.

Claims 1-7, 9-11, and 17-26 lack an inventive step under PCT Article 33(3) as being obvious over Alberto et al (WO 98/43848) because Alberto et al disclose a method of preparing a compound of formula $\text{fac-}[\text{M}(\text{CO})_3(\text{OH}_2)_3]^+$ wherein M is Mn, ^{99m}Tc , ^{186}Re , or ^{188}Re . The compounds are prepared by reacting a metal in the permethylate form with carbon monoxide and a reducing agent, and optionally, a stabilizing agent. In addition, the compounds may be prepared with the aid of amino acids, peptides, proteins, sugars, small receptor binding molecules, and body cells (see entire document, especially, abstract; page 9, Table 1; pages 14-17, claims 1-14). Hence, both Applicant and Alberto et al disclose a method of preparing a compound encompassed by formula I as set forth in Applicant's independent claim 1.

Claims 8, 12-16, 27, and 28 meet the criteria set out in PCT Article 33 (2)-(3) because the prior art does not teach or fairly suggest the use of aminopolycarboxylate chelates as disclosed by Applicant.

INTERNATIONAL SEARCH REPORT

Internat. Classification No.
PCT/US 00/17813

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07F13/00 A61K51/04 //A61K103:10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07F A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ALBERTO, ROGER ET AL: "A Novel Organometallic Aqua Complex of Technetium for the Labeling of Biomolecules: Synthesis of ^{99m} Tc(OH ₂) ₃ (CO) ₃ !+ from ^{99m} TcO ₄ !- in Aqueous Solution and Its Reaction with a Bifunctional Ligand" J. AM. CHEM. SOC., vol. 120, no. 31, 1998, pages 7987-7988, XP002149527	1,6-11, 13-16
X	page 7987	1-3
X	page 7988	6-16
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

6 October 2000

Date of mailing of the international search report

31/10/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo.nl,
Fax: (+31-70) 340-3016

Authorized officer

Bader, K

INTERNATIONAL SEARCH REPORT

Internat. Classification No.
PCT/US 00/17813

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 48848 A (ALBERTO ROGER ; SCHIBLI ROGER (CH); EGLI ANDRE (CH); MALLINCKRODT M) 5 November 1998 (1998-11-05) cited in the application figure 1 page 9; table 1 page 16 -page 17; claims 13,14 ---	1-28
X	ALBERTO, ROGER ET AL: "Metal carbonyl syntheses XXII. Low pressure carbonylation of 'MOC14!- and 'MO4!-: the technetium(I) and rhenium(I) complexes 'NEt4!2'MC13(CO)3!'" J. ORGANOMET. CHEM., vol. 493, no. 1-2, 1995, pages 119-127, XP002149528 page 123 -page 121 page 125 ---	1-3
P,X	EP 1 013 642 A (SCHERING AG) 28 June 2000 (2000-06-28) examples 1-9 -----	1-28

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.
PCT/US 99/17813

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9848848 A	05-11-1998	EP 0879606 A	25-11-1998
		AU 7141398 A	24-11-1998
		BR 9809409 A	13-06-2000
		EP 1019095 A	19-07-2000
		NO 995160 A	13-12-1999
		PL 336382 A	19-06-2000
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EP 1013642 A	28-06-2000	DE 19860289 A	29-06-2000
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PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1328 WO	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 17813	International filing date (day/month/year) 28/06/2000	(Earliest) Priority Date (day/month/year) 29/06/1999
Applicant MALLINCKRODT INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

GROUP(VII) TRANSITION-METAL COMPLEXES WITH MULTIDENTATE AMINOPOLYCARBOXYLATE LIGANDS AND A KIT FOR PRODUCING THEM

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/17813

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07F13/00 A61K51/04 //A61K103:10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07F A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EP0-Internal

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X	page 7987	1-3
X	page 7988 --- -/--	6-16



Further documents are listed in the continuation of box C.



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- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

6 October 2000

Date of mailing of the international search report

31/10/2000

Name and mailing address of the ISA

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Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bader, K

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/17813

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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P, X	EP 1 013 642 A (SCHERING AG) 28 June 2000 (2000-06-28) examples 1-9 -----	1-28

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/17813

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9848848 A	05-11-1998	EP 0879606 A	25-11-1998
		AU 7141398 A	24-11-1998
		BR 9809409 A	13-06-2000
		EP 1019095 A	19-07-2000
		NO 995160 A	13-12-1999
		PL 336382 A	19-06-2000
<hr/>			
EP 1013642 A	28-06-2000	DE 19860289 A	29-06-2000
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